matter at a later time or in a later filed divisional, continuation or continuation-in-part application.

Upon entry of the amendment, claims 26-39 are pending in the instant application.

II. Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

Claim 8 was rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a sulfotransferase gene knockout mouse exhibiting hyperactive and aggressive behavior, does not reasonably provide enablement for any other sulfotransferase gene knockout non-human animals without said phenotype. Applicants respectfully traverse this rejection. In view of the cancellation of claim 8, the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is no longer relevant .

Claims 17-21 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification, while being enabling for a homozygous sulfotransferase knockout mouse lacking production of functional sulfotransferase protein, does not reasonably provide enablement for a heterozygous sulfotransferase knockout mouse or a sulfotransferase gene disrupted mouse. The Examiner asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicants respectfully traverse this rejection. However, in light of the cancellation of claims 17-21, the rejection under 35 U.S.C. § 112, first paragraph, is moot.

Applicants submit that new claims 26-39 are fully enabled by the teachings of the specification. As the rejections under 35 U.S.C. § 112, first paragraph, of claims 8, 17-21 are no longer relevant as a result of the cancellation of these claims, and new claims 26-39 are fully enabled by the teachings of the specification, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-4, 9, 10, and 17-21 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Particularly, claims 1-4 and 10 were rejected based upon the arrangement of the targeting construct. Claims 9 and 21 were rejected under 35 U.S.C. § 112, second paragraph, on the grounds that the word "derived" renders the claim indefinite. Claims 17-21 were rejected under 35 U.S.C. § 112, second paragraph, on the basis that the word

"activity" renders the claims indefinite. Applicants respectfully traverse each rejection under 35 U.S.C. § 112, second paragraph. However, in light of the cancellation of claims 1-4, 9, 10, and 17-21, each rejection is moot. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Applicants submit that new claims 26-39 are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

C. Rejections under 35 U.S.C. § 103

Claims 1-8 and 10 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over Mansour *et al.*, 1998, *Nature,* 336(24):348-352 ("Mansour") in view of Kong *et al.,* 1993, *Biochimica et Biophysica Acta* 1171:315-318 ("Kong"). Applicants respectfully traverse this rejection. However, in view of the cancellation of claims 1-8 and 10, the rejection under 35 U.S.C. § 103 is no longer relevant.

Applicants submit that new claims 26-39 are non-obvious over the teachings of the prior art references. More particularly, the claimed invention relates to the *in vivo* mammalian characterization of the function of sulfotransferase genes, and provides transgenic animals and cells comprising disruptions in sulfotransferase genes and methods and compositions relating thereto, all which are not obvious in view of the sole or combined teachings and disclosures of the references cited by the Examiner.

According to the Examiner, Mansour teaches a strategy for targeted disruption of the *hprt* and proto-oncogene *int-2* in mice embryonic stem cells, and subsequent generation of knockout mice. The disclosure of Mansour specifically relates to a general method for isolating embryonic stem cells containing a targeted mutation in an endogenous gene. More particularly, Mansour teaches the targeted disruption of the *hprt* gene and the proto-oncogene *int-2* in mouse embryonic stem cells by homologous recombination using targeting constructs specific for these genes.

Kong, as characterized by the Examiner, teaches the cloning of a mouse sulfotransferase gene, mST, from mouse liver, and provides the cloned coding sequence for a sulfotransferase gene. The Examiner asserts that Kong implicates the role of the sulfotransferase in the activation of mutagens and carcinogens.

As described above, the disclosure of Mansour is limited to providing a general approach for isolating embryonic stem cells. As acknowledged by the Examiner, Mansour provides no disclosure or teaching of how to make a sulfotransferase gene targeting construct or a sulfotransferase gene knockout mouse. (See Office Action, page 8). More particularly, Mansour does not teach or suggest a targeting construct containing a DNA sequence homologous to a sulfotransferase gene or methods of producing such a construct as recited in the pending claims. Nor, does Mansour teach a method of producing a transgenic mouse comprising a homozygous disruption in a sulfotransferase gene as claimed by the present invention.

Likewise, Kong does not provide any teaching or suggestion relating to targeted disruptions in the sulfotransferase gene. More particularly, the disclosure of Kong fails to provide any teaching or suggestion that relate to the transgenic animals, cells, tissues, targeting constructs, and methods as recited in the pending claims.

Taken together, the disclosures of Mansour and Kong are absent of any teaching or suggestion of disrupting the sulfotransferase gene, and in particular, are deficient of any teachings or suggestions of the transgenic mice, targeting constructs, tissues, cells, and methods as recited in the pending claims. More particularly, the disclosures of Mansour and Kong, alone or combined, do not teach or suggest in any way the transgenic mice comprising disrupted sulfotransferase gene, wherein such transgenic mice exhibit behavior abnormalities, methods of producing such transgenic mice, targeting constructs, tissues and cells that are related to a disrupted sulfotransferase gene as claimed by the present invention.

As the obviousness rejection is no longer relevant as result of the cancellation of claims 1-8 and 10, and new claims 26-39 are not obvious in view of the teachings of Mansour and Kong, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

It is believed that the claims are in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-855.

Respectfully submitted,

Date: 7/11/02

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